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Scaling and root planing, systemic metronidazole and professional plaque removal in the treatment of chronic periodontitis in a Brazilian population

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Abstract

Objective: The current investigation evaluated the clinical effects of scaling and root planing (SRP) alone or in combination with systemic metronidazole and/or repeated professional removal of supragingival plaque in subjects with chronic periodontitis. Methods: Fourty-four adult subjects (mean age: 45 ± 6 years) with periodontitis were randomly assigned to four treatment groups; a control (C, n = 10) that received SRP and placebo and three test groups treated as follows: Test 1 (T1) (n = 12)received SRP and metronidazole (400 mg t.i.d., M) for 10 days; Test 2 (T2) (n = 12)received SRP, weekly professional supragingival plaque removal for three months (professional cleaning (PC)) and placebo; and Test 3 (T3) (n = 10) received SRP, M and PC. Pocket depth (PD), attachment level (AL), bleeding on probing (BOP) and presence of visible plaque and suppuration were measured at six sites per tooth at baseline and at 90 days post-therapy. Significance of differences over time was determined using the Wilcoxon test, and among groups using ANCOVA. **Results:** A reduction in full-mouth mean clinical parameters was observed at 90 days after all therapies. Sites with baseline PD < 4 mm showed an increase in mean PD in the control group and in mean AL in all treatment groups. Sites with baseline PD of 4-6 mm in subjects who received PC as part of therapy (T2, T3) showed a marked reduction in PD, AL and in the % of sites with BOP. Subjects who received metronidazole (T1 and T3) showed the best clinical response at sites with an initial PD of >6 mm. The major clinical benefit occurred when the combination of SRP, M and PC was used. Group T3 showed the least attachment loss in initially shallow pockets. This group also exhibited the greatest reduction in the % of sites with BOP and suppuration as well as in mean PD and AL at sites with baseline PD>4 mm. **Conclusion:** The data suggest a significant clinical benefit in combining SRP, systemic metronidazole and weekly professional supragingival plaque removal for the treatment of chronic periodontitis.

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Even though several treatments for periodontal diseases have been extensively studied, the ideal form of therapy for these infections has not vet been determined. Scaling and root planing (SRP) is the most common periodontal treatment. The overall results of the studies that evaluated the clinical findings associated with SRP indicate a benefit in terms of reducing inflammation and decreasing probing pocket depth (PD) and attachment level (AL) measurements, especially at deeper sites (Morrison et al. 1980, Badersten et al. 1981, Pihlstrom et al. 1983, Ramfjord et al. 1987, Haffajee et al. 1997). A large number of studies evaluated the effects of combining SRP with systemically administered antimicrobial agents (Loesche et al. 1991, 1992, 2002, Bain et al. 1994, Feres et al. 2001, Herrera et al. 2002, Rooney et al. 2002, Smith et al. 2002) and suggested that the adjunctive use of an antibiotic increases the clinical efficacy of SRP therapy. Other authors did not observe this beneficial effect of the systemic drugs combined with SRP over SRP alone (Giedrys-Leeper et al. 1985, Al-Joburi et al. 1989, Flemmig et al. 1998a, b, Palmer et al. 1996).

Systemically, metronidazole seems to be particularly effective for the treatment of chronic periodontitis patients because of its efficacy against obligate anaerobes (Proctor & Baker, 1971, Loesche et al. 1982). Several investigations have shown positive clinical and microbiological results when metronidazole was used in conjunction with SRP (Loesche et al. 1984, 1991, 1992, 2002, Van Oosten et al. 1987, Söder et al. 1990, Elter et al. 1997, Feres et al. 2001). A meta-analysis of the studies that evaluated the effect of systemic metronidazole as an adjunct to SRP in the treatment of chronic periodontitis suggested that this therapy may offer a clinical benefit over SRP alone in managing pockets of 4 mm or greater (Elter et al. 1997). Other studies have also indicated metronidazole treatment to be more effective in deep pockets than in shallow pockets (Clark et al. 1983, Lekovic et al. 1983, Joyston-Bechal et al. 1984, 1986, Loesche et al. 1984, Sterry et al. 1985). In a study of our group this beneficial clinical effect of metronidazole was seen even in pockets of 4 mm or less (Feres et al. 2001).

Supragingival plaque control is considered a crucial step in maintaining periodontal health. The classical longitudinal studies carried out in Sweden by Lindhe and co-workers in the 1970s and 1980s established the importance of oral hygiene for the success of different types of periodontal therapies. This group of investigators demonstrated that the level of plaque control after treatment was more critical in preserving the periodontal status and preventing recurrence of destructive periodontitis than the mode of initial therapy used (Lindhe & Nyman 1975, Nyman et al. 1975, 1977, Rosling et al. 1976, Rosling 1983, Lindhe & Liljenberg 1984). It is important to emphasize that in many of these studies the subjects received supragingival plaque removal after therapy every 2 weeks for an extended period of time. Nyman et al. (1977) demonstrated that the use of five different techniques for surgical pocket elimination were equally ineffective in preventing recurrence of destructive periodontitis when the subjects exhibited poor plaque control posttherapy. Ximenez-Fyvie et al. (2000) showed that meticulous professional supragingival plaque removal performed weekly during the 3 months after periodontal treatment could lead to beneficial changes in the composition of the subgingival microbiota in subjects with moderate periodontitis who were in a maintenance program.

The studies described above indicate that individually SRP, systemically administered metronidazole or repeated professional supragingival plaque removal were effective in treating chronic periodontitis. A logical question was whether combinations of these therapies might be even more effective in improving periodontal status. Thus, the purpose of the present investigation was to evaluate the effects of SRP alone or in combination with systemically administered metronidazole or repeated professional supragingival plaque removal or both on clinical parameters of periodontal disease in subjects with chronic periodontitis.

Material and Methods Subject population

Sixty Brazilian subjects >34 years of age with chronic periodontitis who had not received periodontal therapy previously were selected for the study. Subjects had at least 20 teeth and a minimum of eight teeth with at least one site with PD and AL between 6 and 10 mm and three sites with PD and AL <4 mm. Exclusion criteria included pregnancy, nursing, and any systemic condition that could affect the progression of periodontal disease or required antibiotic coverage for routine dental therapy. In addition, subjects with a known allergy to metronidazole or who had received antibiotic therapy in the previous 6 months were excluded. Subjects who were unwilling to refrain from alcohol consumption during the antibiotic phase of therapy were also excluded.

Experimental design and treatment

In this randomized, placebo-controlled, clinical study, subjects were screened for suitability, and if accepted, were informed of the nature, potential risks and benefits of study participation. Following the signing of an Ethics Committee-approved informed consent, subjects were entered into the study. During the initial phase, subjects received clinical and microbiological monitoring, instructions in proper home-care techniques and full-mouth SRP performed under local anesthesia (Haffajee et al. 1997). SRP was completed in at most six appointments of approximately 1 h each. Treatment of the entire oral cavity was completed in 14 days. Subsequently, subjects were randomly assigned to one of the following therapeutic groups: Control (C), SRP and placebo; Test 1 (T1), SRP+systemically administered metronidazole (M); Test 2 (T2), SRP+weekly professional supragingival plaque removal (professional cleaning (PC)) and placebo; Test 3 (T3), SRP+M+PC. After the completion of SRP, the adjunctive therapies were initiated (day 0). Subjects in groups T1 and T3 received 400 mg of systemically administered metronidazole three times a day for 10 days. Subjects in groups C and T2 received placebo capsules using the same regimen as the metronidazole therapy. The drug and placebo medications were specifically prepared for use in this study. Compliance was assessed by counting the remaining capsules at day 10 and calling the subject every 2 days during the antibiotic administration phase. Also at day 10 after baseline, a questionnaire concerning adverse effects of metronidazole was filled out by each subject. No severe adverse effects were reported by any of the subjects. Subjects in groups T2 and T3 were seen weekly for professional supragingival plaque removal for 3 months. Supragingival plaque was revealed using disclosing solution. Visible supragingival plaque was removed using scalers on all accessible surfaces followed by polishing of the teeth using a rubber cup and dentifrice. Finally, all interproximal surfaces were cleaned using dental floss. When performing these procedures, care was taken to limit plaque removal to the supragingival area only. All subjects received clinical monitoring and subgingival maintenance scaling at 3 months after therapy.

Clinical monitoring

The clinical monitoring was performed by two calibrated examiners ($\kappa > 0.80$). One examiner performed all clinical measurements in a given subject and treatment was performed by the second clinician. Thus, the monitoring clinician was masked to the treatment protocol. Subjects were clinically monitored prior to therapy and at 90 days post-therapy. Plaque accumulation (0/1), overt gingivitis (0/1), bleeding on probing (BOP) (0/1), suppuration (0/1), probing PD and probing AL were measured at six sites per tooth (mesiobuccal, buccal, distobuccal, distolingual, lingual and mesiolingual) at all teeth excluding third molars at each visit. The probing PD and probing AL measurements were recorded to the nearest millimeter using a North Carolina periodontal probe (Hu-Friedy, Chicago, IL, USA).

Data analysis

Of the 60 subjects selected for the study, 16 were excluded from the data analysis, two had taken another drug during the course of the study (one in group T2 and the other in group T3) and the other 14 subjects failed to return for the follow-up appointment (five in the control group, three in group T1, two in group T2 and four in group T3). Therefore, clinical data for 44 subjects were available for data analysis. The mean % of sites with plaque, gingival redness, BOP and suppuration as well as mean PD and AL were computed for each subject and then averaged across subjects in the four treatment groups at each time point. The significance of differences over time (baseline and 90 days) in each group was sought using the Wilcoxon signed-ranks test. Significance of differences among the treatment groups at baseline were sought using the Kruskal–Wallis test and at 3 months using ANCOVA adjusting for age, smoking status and baseline PD.

Results

The mean baseline clinical parameters for the four subject groups are presented in Table 1. The only parameter that differed among groups at baseline was age. Fig. 1 presents the mean full-mouth values for the clinical parameters at baseline and at 90 days for the four treatment groups. The % of sites exhibiting plaque accumulation, BOP, suppuration as well as mean full-mouth PD and AL were significantly reduced at 90 days post-therapy in all treatment groups. There was a statistically significant difference among groups at 90 days for plaque and BOP with groups T2 and T3 showing greater reductions than groups C and T1. Although not significantly from the other treatment groups, the greatest reduction in mean AL was seen in group T3 that received the combination of therapies.

In order to understand better the effect of the various therapies and to allow more comprehensive comparisons among the four groups, the sites were subset into baseline PD categories of

Table 1. Mean (\pm SEM) full-mouth baseline clinical parameters for the four treatment groups

	Control (SRP), 10	T1 (SRP+M), 12	T2 (SRP+PC), 12	T3 (SRP+M+PC), 10
age (years)*	41 ± 5	50 ± 8	46 ± 6	42 ± 5
% males	30	33	33	30
% sites with				
plaque	81 ± 16	82 ± 13	84 ± 10	77 ± 22
bleeding on probing	74 ± 24	75 ± 14	76 ± 15	75 ± 18
suppuration	11 ± 14	7 ± 11	15 ± 22	12 ± 13
mean pocket depth	4.02 ± 0.73	3.68 ± 0.55	3.89 ± 0.85	4.13 ± 1.11
(mm)				
mean attachment level (mm)	4.47 ± 0.88	4.46 ± 0.80	4.46 ± 1.12	4.59 ± 1.10
% current smokers	30	8	42	30

SRP, scaling and root planing; M, metronidazole; PC, professional cleaning.

*p < 0.05; Kruskal–Wallis test.



Fig. 1. Plots of the full-mouth mean values for the clinical parameters at baseline and at 90 days for the four treatment groups (C, control; T, test). Significance of differences over time was tested using the Wilcoxon signed-ranks test (*p < 0.05, **p < 0.01, ***p < 0.001). The significance of differences among groups at 90 days was tested using ANCOVA adjusting for age, smoking status and baseline pocket depth. SRP, scaling and root planing; M, metronidazole; PC, professional cleaning.

shallow (<4 mm), intermediate (4– 6 mm) and deep (>6 mm), and the analyses repeated. Figs 2–4 present the mean values for each clinical parameter at baseline and at 90 days in the three baseline PD categories for the four treatment groups. A reduction in all clinical parameters was observed at 90 days post-therapy for all PD categories, except for the baseline shallow pockets (<4 mm), which showed an increase in the mean PD in the control group and in mean AL in all treatment groups. This increase in mean AL at 90 days was less marked in the combined therapy group (T3, Fig. 2).

Plaque accumulation differed significantly among the four treatment groups post-therapy for the shallow and intermediate baseline PD categories (Figs 2 and 3). Subjects who received PC (groups T2 and T3) showed a lower % of sites with plaque at 90 days. A significant difference among groups was also observed for BOP in the shallow and intermediate PD categories (<4, 4–



Fig. 2. Plots of the mean values for clinical parameters at baseline and 90 days for sites with baseline pocket depths <4 mm, in the four treatment groups. Significance testing and legends are as described in Fig. 1.



Fig. 3. Plots of the mean values for clinical parameters at baseline and 90 days for sites with baseline pocket depths 4-6 mm in the four treatment groups. Significance testing and legends are as described in Fig. 1.

6 mm). Group T3 subjects showed the greatest reduction in BOP for all PD categories (Figs 2–4).

Fig. 5 presents the mean changes from baseline to 90 days for PD, BOP and AL for the different baseline PD categories. The initially shallow pockets in the control group showed a small increase in mean PD at 3 months posttherapy while the three test groups exhibited a reduction. The mean AL showed a small increase in all treatment groups at 3 months at initially shallow PD sites. There was a decrease in the mean % of sites presenting with BOP for all treatment groups. Even though T3 showed the most beneficial changes for this PD category, the differences observed among groups at the initially shallow pockets were not statistically significant.

The changes observed for mean PD and AL at pockets with an initial PD of 4-6 mm did not differ significantly among groups. However, subjects in group T3 showed the greatest improvement in mean AL post-therapy, followed by the subjects in group T2. The % of sites with BOP was significantly different among groups at the initially 4-6 mm sites. Subjects in groups T2 and T3 showed a more marked reduction in this parameter when compared with groups C and T1. The three test groups (T1, T2 and T3) also showed a somewhat greater reduction in PD when compared with the control group.

At pockets with baseline PD > 6 mm, there was a significant difference among groups for PD reduction. Sites in subjects receiving adjunctive metronidazole, with or without PC (T1 and T3), exhibited a greater mean reduction in PD than groups C and T2. Similar differences among groups were observed for change in AL and BOP, but the differences among groups were not statistically significant.

Discussion

Combined therapies for the treatment of infectious diseases are commonly employed in medicine (Soll, 1996, Stupnicki et al. 1996, Goh et al. 1997, Graham et al. 1997). Combinations of antimicrobial agents have also been successfully employed in the treatment of periodontal infections (Van Winkelhoff et al. 1989, 1992, Pavicic et al. 1994, Winkel, 2001). The combination of systemically administered metronidazole



Fig. 4. Plots of the mean values for clinical parameters at baseline and 90 days for sites with baseline pocket depths > 6 mm in the four treatment groups. Significance testing and legends are as described in Fig. 1.



Fig. 5. Bar charts of the adjusted mean changes in mean pocket depth (PD), mean attachment level and % of sites with bleeding on probing at sites with baseline PD of <4, 4-6 and >6 mm. The bars represent the mean values after adjustment using ANCOVA for age, smoking status and baseline PD. The whiskers represent the SEM. Significance of differences among treatment groups for each parameter was tested using ANCOVA.

or repeated professional supragingival plaque removal with SRP or surgical procedures has been described for the treatment of chronic periodontitis (Lindhe et al. 1983, Westfelt et al. 1983, Joyston-Bechal et al. 1984, Loesche et al. 1984, 1991, 1992, 2002, Van Oosten et al. 1987, Jenkins et al. 1989, Soder et al. 1990, Eisenberg et al. 1991, Noyan et al. 1997, XimenezFyvie et al. 2000, Feres et al. 2001). Since these therapies have different modes of action, their combination may provide a better therapeutic outcome. The aim of this study was to evaluate and compare the clinical efficacy of SRP alone or in combination with systemically administered metronidazole and weekly professional supragingival plaque removal. Even though SRP is the most common periodontal therapy and leads to acceptable clinical results, it seemed likely that its performance could be enhanced in certain subjects by individual or combinations of adjunctive procedures.

In the present investigation, all four therapies led to a significant reduction in mean full-mouth PD and AL at 90 days post-therapy as well as a significant reduction in the % of sites exhibiting plaque, suppuration and BOP. The subjects who received the combined therapy (T3) showed the greatest improvement in mean AL at 90 days when compared with the other groups. When the sites were subset according to baseline PD into shallow (<4 mm), intermediate (4–6 mm) and deep (>6 mm), the results showed that the four therapies produced an increase in mean AL in the baseline shallow PD category. These data are in accord with previous studies that showed that shallow pockets tend to lose attachment after SRP (Hill et al. 1981, Pihlstrom et al. 1981, Lindhe et al. 1982a. Badersten et al. 1987). The attachment loss at the shallow sites was least in group T3 (Figs. 2 and 5). T3 subjects exhibited the greatest reductions in the % sites with BOP and in mean reduction in PD and AL at initially intermediate and deep pockets (Figs. 3-5). In the deep PD category (>6 mm), the PC therapy did not show a benefit over SRP alone. This finding was in accord with the data of Westfelt et al. (1998) who showed little benefit of repeated professional supragingival plaque removal at sites with initially deep periodontal pockets. Subjects who received metronidazole (groups T1 and T3) showed a better clinical improvement when compared with the other groups. This was particularly noticeable for subjects in group T3 who showed the greatest reductions in AL, PD and BOP (Fig. 5). These results are in agreement with other studies that suggested an additional benefit in clinical parameters for initially deep sites, when metronidazole was used as an adjunct to SRP (Lindhe et al. 1983, Van Oosten et al. 1987, Jenkins et al. 1989, Joyston-Bechal et al. 1984, Loesche et al. 1984, 1991, 1992, 2002, Soder et al. 1990, Eisenberg et al. 1991, Noyan et al. 1997, Feres et al. 2001).

An interesting finding in this study was seen at pockets with an initial PD of 4–6 mm. At this PD category, groups T2 and T3 that received weekly PC as part of the therapy showed a greater reduction in AL and, especially in the % of sites presenting BOP when compared with groups T1 and control. The fact that the meticulous professional plaque control after the active phase of periodontal therapy facilitates the maintenance of a healthy periodontium is well documented (Axelsson & Lindhe, 1974, Nyman et al. 1975, Rosling et al. 1976, Westfelt et al. 1983).

The frequency and duration of the professional supragingival plaque removal in this study was the same as that described by Ximenez-Fyvie et al. (2000). They found that weekly professional supragingival plaque removal for 3 months after SRP led to a markedly beneficial change in the composition of the subgingival microbiota in periodontitis subjects in a maintenance program. However, the frequency and duration of PC to obtain optimal results have not been clearly determined. For example, studies in the literature have used other protocols such as professional supragingival plaque removal every 3 weeks for periods of time that varied from 3 to 6 months (Lindhe et al. 1982b, Westfelt et al. 1983) to 2 years (Nyman et al. 1975).

The optimal dose and duration of adjunctive systematically administered metronidazole for the treatment of periodontal infections has also not been determined. The dose and duration of metronidazole administration used in the present investigation was based on the Physicians Desk Reference (Medical Economics Staff, 1992) that recommends 250-500 mg of metronidazole, three times a day, for 7-10 days to treat anaerobic infections. Other studies, however, have used different protocols for metronidazole administration that have demonstrated clinical efficacy (Loesche et al. 1991, 1992, Feres et al. 2001).

The major finding of this study was the suggestion of added clinical benefit in combining SRP, metronidazole and professional supragingival plaque removal (group T3). Subjects receiving this combined therapy showed the most favorable results for all categories of baseline PDs. This combined therapy led to the mildest loss of AL in shallow pockets and to the greatest improvement in clinical parameters at the intermediate and deep periodontal pockets compared with the other treatment groups. However, it will be important to examine microbiological changes and longterm clinical changes in larger groups of subjects to substantiate the clinical usefulness of combined periodontal therapies.

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References

- Al-Joburi, W., Quee, T. C., Lautar, C., Iugovaz, I., Bourgouin, J., Delorme, F. & Chan, E. C. (1989) Effects of adjunctive treatment of periodontitis with tetracycline and spiramycin. *Journal of Periodontology* **60**, 533–539.
- Axelsson, P. & Lindhe, J. (1974) The effect of a preventive programme on dental plaque, gingivitis and caries in schoolchildren. Results after one and two years. *Journal of Clinical Periodontology* 1, 126–138.
- Badersten, A., Nilveus, R. & Egelberg, J. (1981) Effect of nonsurgical periodontal therapy. I. Moderately advanced periodontitis. *Journal of Clinical Periodontology* 8, 57–72.
- Badersten, A., Nilveus, R. & Egelberg, J. (1987) Effect of nonsurgical periodontal therapy (VIII). Probing attachment changes related to clinical characteristics. *Journal of Clinical Periodontology* 14, 425–432.
- Bain, C. A., Beagrie, G. S., Bourgoin, J., Delorme, F., Holthuis, A., Landry, R. G., Roy, S., Schuller, P., Singer, D. & Turnbull, R. (1994) The effects of spiramycin and/or scaling on advanced periodontitis in humans. *Journal of the Canadian Dental Association* **60**, 212–217.
- Clark, D. C., Shenker, S., Stulginski, P. & Schwartz, S. (1983) Effectiveness of routine periodontal treatment with and without adjunctive metronidazole therapy in a sample of mentally retarded adolescents. *Journal of Periodontology* 54, 658–665.
- Eisenberg, L., Suchow, R., Coles, R. S. & Deasy, M. J. (1991) The effects of metronidazole administration on clinical and microbiologic parameters of periodontal disease. *Clinical Preventive Dentistry* 13, 28–34.
- Elter, J. R., Lawrence, H. P., Offenbacher, S. & Beck, J. D. (1997) Meta-analysis of the effect of systemic metronidazole as an adjunct to scaling and root planing for adult periodontitis. *Journal of Periodontal Research* 32, 487–496.
- Feres, M., Haffajee, A. D., Allard, K., Som, S. & Socransky, S. S. (2001) Change in subgingival microbial profiles in adult periodontitis subjects receiving either systemically-administered amoxicillin or metronidazole. *Journal of Clinical Periodontology* 28, 597–609.
- Flemmig, TF., Milian, E., Karch, H. & Klaiber, B. (1998a) Differential clinical treatment outcome after systemic metronidazole and amoxicillin in patients harboring *Actinoba*-

cillus actinomycetemcomitans and/or Porphyromonas gingivalis. Journal of Clinical Periodontology **25**, 380–387.

- Flemming, T. F., Milian, E., Kopp, C., Karch, H. & Klaiber, B. (1998b) Differential effects of systemic metronidazole and amoxicillin on *Actinobacillus actinomycetemcomitans* and *Porphyromonas gingivalis* in intraoral habitats. Journal of Clinical Periodontology 25, 1–10.
- Giedrys-Leeper, E., Selipsky, H. & Williams, B. L. (1985) Effects of short-term administration of metronidazole on the subgingival microflora. *Journal of Clinical Periodontology* **12**, 797–814.
- Goh, K. L., Parasakthi, N., Chuah, S. Y. & Toetsch, M. (1997) Combination amoxycillin and metronidazole with famotidine in the eradication of *Helicobacter pylori* – a randomized, double-blind comparison of a three times daily and twice daily regimen. *European Journal of Gastroenterology Hepatology* 9, 1091–1095.
- Graham, D. Y., Hoffman, J., el-Zimaity, H. M., Graham, D. P. & Osato, M. (1997) Twice a day quadruple therapy (bismuth subsalicylate, tetracycline, metronidazole plus lanzoprazole) for treatment of *Helicobacter pylori* infection. *Alimentary Pharmacology and Therapeutics* **11**, 935–938.
- Haffajee, A. D., Cugini, M. A., Dibart, S., Smith, C., Kent, R. L. Jr. & Socransky, S. S. (1997) The effect of SRP on the clinical and microbiological parameters of periodontal diseases. *Journal of Clinical Periodontology* 24, 324–334.
- Herrera, D., Sanz, M., Jepsen, S., Needleman, I. & Roldan, S. (2002) A systematic review on the effect of systemic antimicrobials as an adjunct to scaling and root planing in periodontitis patients. *Journal of Clinical Periodontology* **29** (Suppl. 3), 136–159.
- Hill, R. W., Ramfjord, S. P., Morrison, E. C., Appleberry, E. A., Caffesse, R. G., Kerry, G. J. & Nissle, R. R. (1981) Four types of periodontal treatment compared over two years. *Journal of Periodontology* 52, 655–662.
- Jenkins, W. M., MacFarlane, T. W., Gilmour, W. H., Ramsay, I. & MacKenzie, D. (1989) Systemic metronidazole in the treatment of periodontitis. *Journal of Clinical Periodontology* 16, 443–450.
- Joyston-Bechal, S., Smales, F. C. & Duckworth, R. (1984) Effect of metronidazole on chronic periodontal disease in subjects using a topically applied chlorhexidine gel. *Journal* of Clinical Periodontology **11**, 53–62.
- Joyston-Bechal, S., Smales, F. C. & Duckworth, R. (1986) A follow-up study 3 years after metronidazole therapy for chronic periodontal disease. *Journal of Clinical Periodontology* 13, 944–949.
- Lekovic, V., Kenney, E. B., Carranza, F. A. Jr. & Endres, B. (1983) The effect of metronidazole on human periodontal disease. A clinical and bacteriological study. *Journal* of *Periodontology* 54, 476–480.
- Lindhe, J. & Liljenberg, B. (1984) Treatment of localized juvenile periodontitis. Results after

5 years. Journal of Clinical Periodontology 11. 399-410.

- Lindhe, J., Liljenberg, B., Adielson, B. & Borjesson, I. (1983) Use of metronidazole as a probe in the study of human periodontal disease. Journal of Clinical Periodontology 10 100-112
- Lindhe, J. & Nyman, S. (1975) The effect of plaque control and surgical pocket elimination on the establishment and maintenance of periodontal health. A longitudinal study of periodontal therapy in cases of advanced disease. Journal of Clinical Periodontology 2. 67-79.
- Lindhe, J., Nyman, S. & Karring, T. (1982a) Scaling and root planing in shallow pockets. Journal of Clinical Periodontology 9, 415-418.
- Lindhe, J., Socransky, S. S., Nyman, S., Haffajee, A. & Westfelt, E. (1982b) "Critical probing depths" in periodontal therapy. Journal of Clinical Periodontology 9, 323-336.
- Loesche, W. J., Giordano, J. R., Hujoel, P., Schwarcz, J. & Smith, B. A. (1992) Metronidazole in periodontitis: reduced need for surgery. Journal of Clinical Periodontology 19. 103-112.
- Loesche, W. J., Giordano, J. R., Soehren, S. & Kaciroti, N. (2002) The nonsurgical treatment of patients with periodontal disease: results after five years. Journal of the American Dental Association 133, 311-320.
- Loesche, W. J., Schmidt, E., Smith, B. A., Morrison, E. C., Caffesse, R. & Hujoel, P. P. (1991) Effects of metronidazole on periodontal treatment needs. Journal of Periodontology 62, 247-257.
- Loesche, W. J., Syed, S. A., Laughon, B. E. & Stoll, J. (1982) The bacteriology of acute necrotizing ulcerative gingivitis. Journal of Periodontology 53, 223–230.
- Loesche, W. J., Syed, S. A., Morrison, E. C., Kerry, G. A., Higgins, T. & Stoll, J. (1984) Metronidazole in periodontitis. I. Clinical and bacteriological results after 15 to 30 weeks. Journal of Periodontology 55, 325-335
- Medical Economics Staff (1992) Physicians Desk Reference. 46th ed. pp. 2170-2174. Montvale: Medical Economics.
- Morrison, E. C., Ramfjord, S. P. & Hill, R. W. (1980) Short-term effects of initial, nonsurgical periodontal treatment (hygienic phase). Journal of Clinical Periodontology 7, 199-211
- Noyan, U., Yilmaz, S., Kuru, B., Kadir, T., Acar, O. & Buget, E. (1997) A clinical and microbiological evaluation of systemic and local metronidazole delivery in adult periodontitis patients. Journal of Clinical Periodontology 24, 158-165.
- Nyman, S., Lindhe, J. & Rosling, B. (1977) Periodontal surgery in plaque-infected dentitions. Journal of Clinical Periodontology 4, 240-249
- Nyman, S., Rosling, B. & Lindhe, J. (1975) Effect of professional tooth cleaning on

healing after periodontal surgery. Journal of Clinical Periodontology 2, 80-86.

- Pavicic, M. J., van Winkelhoff, A. J., Douque, N. H., Steures, R. W. & de Graaff, J. (1994) Microbiological and clinical effects of metronidazole and amoxicillin in Actinobacillus actinomycetemcomitans-associated periodontitis. A 2-year evaluation. Journal of Clinical Periodontology 21, 107-112.
- Palmer, R. M., Watts, T. L. & Wilson, R. F. (1996) A double-blind trial of tetracycline in the management of early onset periodontitis. Journal of Clinical Periodontolog 23, 670-674.
- Pihlstrom, B. L., McHugh, R. B., Oliphant, T. H. & Ortiz-Campos, C. (1983) Comparison of surgical and nonsurgical treatment of periodontal disease. A review of current studies and additional results after 61/2 years. Journal of Clinical Periodontology 10, 524-541.
- Pihlstrom, B. L., Ortiz-Campos, C. & McHugh, R. B. (1981) A randomized four-years study of periodontal therapy. Journal of Periodontology 52, 227-242.
- Proctor, D. B. & Baker, C. G. (1971) Treatment of acute necrotizing ulcerative gingivitis with metronidazole. Journal of the Canadian Dental Association 37, 376-380.
- Ramfjord, S. P., Caffesse, R. G., Morrison, E. C., Hill, R. W., Kerry, G. J., Appleberry, E. A., Nissle, R. R. & Stults, D. L. (1987) 4 modalities of periodontal treatment compared over 5 years. Journal of Clinical Periodontology 14, 445-452.
- Rooney, J., Wade, W. G., Sprague, S. V., Newcombe, R. G. & Addy, M. (2002) Adjunctive effects to non-surgical periodontal therapy of systemic metronidazole and amoxycillin alone and combined. A placebo controlled study. Journal of Clinical Periodontology 29, 342-350.
- Rosling, B. (1983) A comparison of various surgical methods for the treatment of periodontal disease. Deutsche Zahnarztliche Zeitschrift 38, 836-841.
- Rosling, B., Nyman, S., Lindhe, J. & Jern, B. (1976) The healing potential of the periodontal tissues following different techniques of periodontal surgery in plaquefree dentitions. A 2-year clinical study. Journal of Clinical Periodontology 3, 233-250.
- Smith, S. R., Foyle, D. M., Daniels, J., Joyston-Bechal, S., Smales, F. C., Sefton, A. & Williams, J. (2002) A double-blind placebocontrolled trial of azithromycin as an adjunct to non-surgical treatment of periodontitis in adults: clinical results. Journal of Clinical Periodontology 29, 154-161.
- Soder, P. O., Frithiof, L., Wikner, S., Wouters, F., Engstrom, P. E., Rubin, B., Nedlich, U. & Soder, B. (1990) The effect of systemic metronidazole after non-surgical treatment in moderate and advanced periodontitis in young adults. Journal of Periodontology 61, 281 - 288
- Soll, A. H. (1996) Consensus conference. Medical treatment of peptic ulcer disease.

Practice guidelines. Practice Parameters Committee of American College of Gastroenterology. Journal of the American Medical Association 275, 622-629.

- Sterry, K. A., Langeroudi, M. & Dolby, A. E. (1985) Metronidazole as an adjunct to periodontal therapy with sub-gingival curettage. British Dental Journal 158, 176-178.
- Stupnicki, T., Taufer, M., Denk, H., Ratschek, M., Spath, P. & Graf, K. (1996) Triple therapy with sucralfate, amoxycillin and metronidazole for healing duodenal ulcer and eradicating Helicobacter pylori infection. Alimentary Pharmacology and Therapeutics 10, 193-197.
- van Oosten, M. A., Mikx, F. H. & Renggli, H. H. (1987) Microbial and clinical measurements of periodontal pockets during sequential periods of non-treatment, mechanical debridement and metronidazole therapy. Journal of Clinical Periodontology 14, 197-204.
- van Winkelhoff, A. J., Rodenburg, J. P., Goene, R. J., Abbas, F., Winkel, E. G. & de Graaff, J. (1989) Metronidazole plus amoxycillin in the treatment of Actinobacillus actinomycetemcomitans-associated periodontitis. Journal of Clinical Periodontology 16, 128-131.
- van Winkelhoff, A. J., Tijhof, C. J. & de Graaff, J. (1992) Microbiological and clinical results of metronidazole plus amoxicillin therapy in Actinobacillus actinomycetemcomitans-associated periodontitis. Journal of Periodontology 63, 52-57.
- Westfelt, E., Nyman, S., Socransky, S. S. & Lindhe, J. (1983) Significance of frequency of professional tooth cleaning for healing following periodontal surgery. Journal of Clinical Periodontology 10, 148-156.
- Westfelt, E., Rylander, H., Dahlén, G. & Lindhe, J. (1998) The effect of supragingival plaque control on the progression of advanced periodontal disease. Journal of Clinical Periodontology 25, 536-541.
- Winkel, E. G., van Winkelhoff, A. J., Timmerman, M. F., van der Velden, U. & van der Weijden, G. A. (2001) Amoxicillin plus metronidazole in the treatment of adult periodontitis patients. A double-blind placebo-controlled study. Journal of Clinical Periodontology 28, 296-305.
- Ximenez-Fyvie, L. A., Haffajee, A. D., Som, S., Thompson, M., Torresyap, E. & Socransky, S. S. (2000) The effect of repeated professional supragingival plaque removal on the composition of the supra - and subgingival microbiota. Journal of Clinical Periodontology 27, 637-647.

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